

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2004/011651

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 505 135 A (MERCK & CO. INC) 23 September 1992 (1992-09-23)	
A	CHEUNG M C ET AL: "Comparison of the effects of triphasic oral contraceptives with desogestrel or levonorgestrel on apolipoprotein A-I-containing high-density lipoprotein particles" METABOLISM, CLINICAL AND EXPERIMENTAL, W.B. SAUNDERS CO., PHILADELPHIA, PA, US, vol. 48, no. 5, May 1999 (1999-05), pages 658-664, XP004538649 ISSN: 0026-0495	

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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the International filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the International filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*G\* document member of the same patent family

Date of the actual completion of the International search

11 February 2005

Date of mailing of the International search report

09.05.2005

Name and mailing address of the ISA

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 03/035670 A (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA; MEHRABIAN, MARGARETE; ALL) 1 May 2003 (2003-05-01) page 5, lines 4-7,16,25-28 page 25, lines 9-15	1-9,14, 18,22, 29-36
Y	IN ET AL: "NATURALLY OCCURRING MUTATIONS IN THE HUMAN 5-LIPOXYGENASE GENE PROMOTER THAT MODIFY TRANSCRIPTION FACTOR BINDING AND REPORTER GENE TRANSCRIPTION" JOURNAL OF CLINICAL INVESTIGATION, NEW YORK, NY, US, vol. 99, no. 5, 1997, pages 1130-1137, XP002145101 ISSN: 0021-9738 figures 4,5 the whole document	1-9,14, 18,22, 29-36
A	ARCHACKI STEPHEN R ET AL: "Identification of new genes differentially expressed in coronary artery disease by expression profiling." PHYSIOLOGICAL GENOMICS, vol. 15, January 2004 (2004-01), pages 65-74, XP002315209 ISSN: 1094-8341	
A	MA JUN ET AL: "Gene profiling identifies secreted protein transcripts from peripheral blood cells in coronary artery disease." JOURNAL OF MOLECULAR AND CELLULAR CARDIOLOGY, vol. 35, no. 8, August 2003 (2003-08), pages 993-998, XP002315210 ISSN: 0022-2828	
X	YOU SUN-AH ET AL: "Proteomic approach to coronary atherosclerosis shows ferritin light chain as a significant marker: Evidence consistent with iron hypothesis in atherosclerosis." PHYSIOLOGICAL GENOMICS, vol. 13, July 2003 (2003-07), pages 25-30, XP002315211 ISSN: 1094-8341 abstract the whole document	37-42, 44,47, 51, 55-58, 60-62, 78,82-84
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International Application No

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>KOENIG W ET AL: "C-REACTIVE PROTEIN, A SENSITIVE MARKER OF INFLAMMATION, PREDICTS FUTURE RISK OF CORONARY HEART DISEASE IN INITIALLY HEALTHY MIDDLE-AGES MEN. RESULTS FROM THE MONICA (MONITORING TRENDS AND DETERMINANTS IN CARDIOVASCULAR DISEASE) AUGSBURG COHORT STUDY, 1984 TO 1992" CIRCULATION, AMERICAN HEART ASSOCIATION, DALLAS, TX, US, vol. 99, 10 January 1999 (1999-01-10), pages 237-242, XP000943357 ISSN: 0009-7322</p>	
A	<p>WILSON P W F ET AL: "Prediction of Coronary Heart Disease Using Risk Factor Categories" CIRCULATION, AMERICAN HEART ASSOCIATION, DALLAS, TX, US, vol. 97, 1998, pages 1837-1847, XP002226231 ISSN: 0009-7322</p>	
A	<p>WILSON P W F: "ESTABLISHED RISK FACTORS AND CORONARY ARTERY DISEASE: THE FRAMINGHAM STUDY" AMERICAN JOURNAL OF HYPERTENSION, NEW YORK, NY, US, vol. 7, no. 7, PART 2, July 1994 (1994-07), pages 7S-12S, XP009042593</p>	

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/011651

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0505135	A	23-09-1992	US 5151365 A	29-09-1992
			US 5182298 A	26-01-1993
			US 5166217 A	24-11-1992
			CA 2063230 A1	19-09-1992
			EP 0505135 A2	23-09-1992
			JP 8134059 A	28-05-1996
			US 5244795 A	14-09-1993
WO 03035670	A	01-05-2003	CA 2465261 A1	01-05-2003
			EP 1448794 A2	25-08-2004
			WO 03035670 A2	01-05-2003
			US 2004209288 A1	21-10-2004

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP2004/011651

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-9, 14, 18, 22, 29-36, 37-39, 41, 42, 44, 47, 51, 56-58, 60-62, 78, 82-84 (partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box II.2

## Claims Nos.:

13,15,16,19,20,23,24,26,40,43,45,48,49,52,53,55,59,63-77,79-81,87,88

The claims of the present application refer to Tables 6 (160 entries), 7 (8 entries), 9 (19 entries), 10 (15 entries) and 11 (15 entries) whereby "at least one gene" or "one or more peptide" or "at least two to eight sequences" etc. from one or more tables are claimed (see, for example, claims 1, 6, 7, 10, 14, 27, 40, 59 etc.).

The entries of Tables 7, 9 and 10 are subgroups of sequences of those sequences listed in Table 6 (description, pages 40, 45 and 46). The entries in Table 11, however, have been obtained by a different method and are not a subgroup of any of the other tables (description, Example 4).

In view of the high number of entries in each table, an extremely large number of possible combinations is claimed. In fact, the claims contain so many options that a lack of clarity and conciseness within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search over the whole scope of the claims impossible. The search has thus been carried out for those parts of the application which do appear to be clear and concise, namely the individual nucleic acid/peptides referred to in any of the said tables and to those specific combinations whereby ALL entries of a single table are claimed (e.g. claims 21, 25, 27 etc.). Consequently, claims referring to "at least two of ..." or a "plurality of ..." have not been searched (claims 15, 19, 20, 23, 24, 26, 45, 48, 49, 52, 53, 55, 66, 69, 72, 74). Also, claims referring to "at least one member" of Table X "and/or at least one member" of Table Y have been searched to the extent as they refer to a combination with "or" and not with regard to the combination with "and", provided that the tables combined are selected from Tables 6, 7, 9 and 10. A combination of elements of table 11 with an element of any other table has not been searched.

It is to note that the present application appears not to disclose preferred combinations between any of the tables on which to which a meaningful search could have been limited.

The Applicant is to note that should he pay additional search fees for further inventions, than the above objections may also be raised in relation to these further inventions.

Claims 75-77,79-81 refers to methods of treatment comprising an "agent" and the use of the said "agent" for the preparation of a medicament. The agent referred to in the said claims is defined by the result to be achieved, such as a particular activity on a particular gene, without providing, however, any structural features of the agent as such. The description, moreover, appears not to disclose a single example of an agent. The subject-matter of the said claims 75-81 is therefore not defined by technical features and is therefore so unclear (Art 6 PCT) that no meaningful search can be carried out.

In conclusion, the following claims were included into the non-unity

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

objection:

fully or partly:

1-12,14,17,18,21,22,25,27-39,41,42,44,46,47,50,51,54,56-58,60-62,78,82-85

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Inventions 1-160: claims

1-9,14,18,22,29-36,37-39,41,42,44,47,51,56-58,60-62,78,82-84  
(fully)

Method for identifying or predicting the predisposition of coronary artery disease (CAD) in a subject, for monitoring a subject identified as having CAD, for screening candidate agents for use in a treatment of CAD, for treating a subject suffering from CAD, the use of a substance for the preparation of a medicament for CAD and kits for some of the above methods, comprising determining the level of gene expression of the 1./2./3. ... 159./160. gene selected from table 6, 7, 9 or 10 (the genes referred to in tables 7, 9 or 10 are subsets of those in table 6).

Invention 161: claims 17,29-36,46 (fully);  
1-6,9,37,39,41,42,44(partly)

Methods for identifying or predicting coronary artery disease (CAD) in a subject, for monitoring a subject identified as having CAD, for monitoring progression of CAD, for screening for agents for use in the treatment of CAD, for treating subjects having CAD, use of agents for the preparation of medicaments for treating CAD and kits for the above methods comprising determining the level of all genes defined in Table 7.

Invention 162: claims 21,29-36,50(fully);  
1-5,7,9,18,38,39,41,42,47(partly)

Methods for monitoring coronary artery disease (CAD) in a subject, for screening candidate agents for use in a treatment of CAD, for treating a subject suffering from CAD, the use of a substance for the preparation of a medicament for CAD and kits for some of the above methods, comprising determining the level of gene expression of all genes of Table 9.

Invention 163: claims 25,29-36,54(partly);  
1-5,8,9,22,38,39,41,42,51(fully)

Methods for monitoring coronary artery disease (CAD) in a subject, for screening candidate agents for use in a treatment of CAD, for treating a subject suffering from CAD, the use of a substance for the preparation of a medicament for CAD and kits for some of the above methods, comprising determining the level of gene expression of at least one of all genes of Table 10.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Inventions 164-183: claims 10-12,28,29-36,85,86(fully)

Method for identifying or predicting the predisposition of coronary artery disease (CAD) in a subject, for monitoring a subject identified as having CAD, for screening candidate agents for use in a treatment of CAD, for treating a subject suffering from CAD, the use of a substance for the preparation of a medicament for CAD and kits for some of the above methods, comprising determining the level of protein expression of the 1./2./3. ... 19. protein of table 11.

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Invention: 184: claims 27,28,29-36(fully); 10-12(partly)

Method for identifying or predicting the predisposition of coronary artery disease (CAD) in a subject, for monitoring a subject identified as having CAD, for screening candidate agents for use in a treatment of CAD, for treating a subject suffering from CAD, the use of a substance for the preparation of a medicament for CAD and kits for some of the above methods, comprising determining the level of protein expression of all proteins of table 11.

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